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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,190	06/24/2003	Maria Elena Garcia Armenta	222992	1009

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LEYDIG VOIT & MAYER, LTD
TWO PRUDENTIAL PLAZA, SUITE 4900
180 NORTH STETSON AVENUE
CHICAGO, IL 60601-6731

EXAMINER	
WANG, SHENGJUN	

ART UNIT	PAPER NUMBER
1617	

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05/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,190	GARCIA ARMENTA ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' remarks submitted February 6, 2008 is acknowledged.

Claim Objections

1. Claims 9-11 are objected to because of the following informalities: "Claim 1" recited in claims appears to be a typographic error of "claim 8". Appropriate correction is required.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raffa et al. (EP 0 546 676) and Caruso (U.S. 5,919,826), and in further view of Saslawski et al. (US 6,372,255), Forrest et al. and Physicians' Desk Reference.

3. Raffa et al. teaches a pharmaceutical composition comprising a tramadol compound and a non-steroid anti-inflammatory drug (NSAID), and the method of using the same for treating pain. The composition provides benefits, such as less opioid side effects and synergistic pharmacological effects. See the abstract. Tramadol compounds may be any salts of tramadol, such as hydrochloride salt. See, particularly, page 3, lines 26-34. Any of the well-known NSAID may be used in the composition. The ratio of tramadol to NSAID is in the range of 1:1 to1:200. The composition may be prepared according to conventional pharmaceutical compounding techniques. Known pharmaceutical carrier and other excipients may be used in the composition

and the composition may be in the any of the known dosage forms, such as powders, capsules, etc. See, particularly, page 3, line 50 to page 4, line 49. Caruso discloses a pharmaceutical composition for treating pain comprising tramadol and a NSAID, wherein ketorolac as one of the preferred NSAID. See, particularly, col. 6, lines 12-20, and claims 5 and 6.

4. The primary references do not teach expressly the particular carrier and excipients recited herein, or the particular salts of tramadol and ketorolac, or the amounts of each of the ingredients in the composition.

5. However, Saslawski et al. teaches that the particular carrier and excipients herein are well-known pharmaceutical carrier and excipients. See, particularly, column 5, line 37 to column 6, line 67. Forest et al. teaches that ketorolac is particularly known to be useful for pain management and is known to yield a synergistic effect when combined with opioid. See, particularly, the abstract. Further, Physicians' Desk Reference reveals that tramadol chloride and ketorolac tromethamine are the known salt currently employed clinically for tramadol and ketorolac.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to make a pharmaceutical composition for treating pain comprising ketorolac tromethamine and tramadol hydrochloride as herein recited. A person of ordinary skill in the art would have been motivated to make a pharmaceutical composition for treating pain comprising ketorolac tromethamine and tramadol hydrochloride as herein recited because tramadol is known to be used with NSAID to yield synergistic analgesic effect, and ketorolac, a well known NSAID is known to potentiate analgesia are known to be used together and to provide benefit such as less opioid side effects and pharmacological

synergistic effects, and ketorolac tromethamine and tramadol hydrochloride are the particularly salts used clinically. Note the optimization of a result effective parameter, e.g., the amount of therapeutical agents, or the amounts of the well-known pharmaceutical excipients, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215. Further note that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Response to the Arguments

Applicants' remarks submitted February 9, 2008 have been fully considered, but are not persuasive.

Applicants' argue that it is unpredictable that combining tramadol with NSAID would yield a synergistic analgesia effect. The arguments are unpersuasive. Applicants cited a single example of combination of tramadol and refecoxib showing no synergistic effect. However, as shown by the cited references, ketorolac is particularly known to yield synergistic effect when combined with opioid.

6. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

7. Applicant's attention is further directed to KSR vs. Teleflex, where the court states: "When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. **If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.**" The prior art teach that tramadol (an atypical opioid) is known to be used with a NSAID for treatment of pain, and Ketorolac (a NSAID) is known to be used for treatment of with an opioid. One of ordinary skill in the art would have motivated to combine tramadol and ketorolac for treatment of pain with a reasonable expectation of the synergistic benefit known in the art.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shengjun Wang/
Primary Examiner, Art Unit 1617